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TREATMENT OF ATHEROSCLEROSIS THROUGH PENETRATION OF PLAQUE BY SOFT ROBOTS

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ABSTRACT

A substance called plaque accumulates on the inner walls of arteries due to the consumption of foods high in cholesterol, saturated fats, and so on. The accumulation of plaque deposits leads to a condition known as atherosclerosis, which results in the narrowing and hardening of the arteries. This can lead to coronary artery disease, carotid artery disease, peripheral artery disease, chest pain (also referred to as angina pectoris), heart attack, heart failure, and many more medical complications. The current treatments for atherosclerosis include coronary artery bypass grafting (CABG), angioplasty, percutaneous coronary intervention (PCI), and a number of health and lifestyle changes that could prevent atherosclerotic plaque buildup. These surgeries either involve opening clogged arteries to prevent constriction or directing the blood away from the blocked artery. In both these cases, risks of bleeding, bruising, and complete recovery are prevalent. Therefore, a procedure in which a robot could remove the plaque from the walls of the arteries would greatly increase the success of the treatment and perhaps reduce the risks. This paper intends to review the newly proposed robots for the treatment of atherosclerosis, some of which are magnetically manipulated to drill the plaque to remove it from the arterial wall, and others that are meant to melt the plaque while still preserving the physical integrity of the arteries.

KEYWORDS: Plaque, Arteries, Atherosclerosis, Coronary, Heart

INTRODUCTION

Arterial plaque (atheroma) is a sticky substance composed of fat, calcium, cholesterol, cellular waste, fibrin, and other materials. Atheroma is found in the blood and builds up inside the arteries, causing them to narrow and harden over time. The artery walls grow thicker and harder with time due to the consistent build-up of plaque. Due to the accumulation of plaque, there is a high likelihood of blood clot formation as well as the complete blockage of an artery. The deposition of plaque also limits the flow of rich oxygen blood to your body. This accumulation can occur in any artery in the body, from the head to the toe, and can lead to the development of atherosclerosis, a condition that can cause angina, a heart attack, coronary artery disease, and possibly even heart failure (Miller, 2024).

It is believed that it begins with damage to the artery's inner lining (epithelium). There are several risk factors that can culminate in atherosclerosis such as a family history of heart disease, a lack of physical activity, smoking, high blood pressure, high cholesterol, diabetes, obesity, stress, and anxiety.

There are 4 stages of atherosclerosis:

- The first stage involves endothelial damage. This is when the lining of your artery suffers trauma.
- The second stage involves the formation of a fatty streak, a yellow streak comprising dead foam cells at the site of endothelial damage.
- In the third stage, plaque continues to build up. Fibrous Over the plaque, a fibrous cap composed of smooth muscle cells grows. This cap keeps plaque fragments from splintering off and entering your blood ("Atherosclerosis", n.d.).
- In the fourth stage, the blood in the artery with the plaque clots because of plaque rupture. This means that the fibrous cap mentioned above breaks off. The blood can also clot due to plaque erosion, in which the cap is unaffected but the surrounding endothelial cells get worn away.

Atherosclerosis can ultimately cause a multitude of complications, such as carotid artery disease, coronary artery disease, heart attack, stroke, and several others.

The surgeries or procedures to treat atherosclerosis are:

1. **Coronary Artery Bypass Grafting (CABG):** This surgery is particularly for the treatment of atherosclerosis in the coronary artery, and involves bypassing the blocked segment of the coronary artery. This is done by using healthy blood vessels from other parts of the body. These blood vessels are referred to as grafts. The ends of the graft are attached above and below the blocked artery. This has the effect of establishing a new passage for the smooth flow of the blood which bypasses the arteries with plaque accumulation.
2. **Angioplasty:** In this procedure, arteries constricted due to atherosclerosis are opened to improve the flow of blood. The doctor, typically an interventional cardiologist, moves the plaque to the sides of the arterial wall by inflating a small balloon in the artery. Sometimes, the balloon is coated with medicine to facilitate arterial healing (*Peripheral Artery Disease - Treatment | NHLBI, NIH, n.d.*). Subsequently,

a stent is inserted into the artery to keep it open after removing the balloon.

This provides a clear passageway for the circulation of blood.

These two surgical procedures are some of the most popular treatments for the blockage and narrowing of arteries due to the accumulation of plaque among many others, such as Carotid artery surgery and endarterectomy.

Despite their popularity, these surgeries have their respective risks.

The risks of CABG include bleeding during or after the surgery, infection at the incision site, stroke, renal failure, and even death (Bachar and Manna, n.d.). Moreover, CABG involves a long recovery period, which requires hospitalization for several days to weeks.

Another major risk associated with CABG is the failure of the graft.

In a study by Mario Gaudino on graft failure after CABG, seven trials were conducted consisting of 4413 patients, which corresponds to 13613 grafts. Graft failure occurred in 1487 patients(33.7%) and 2190 grafts (16.6%). Graft failure can consequently increase the risk of myocardial infarction.

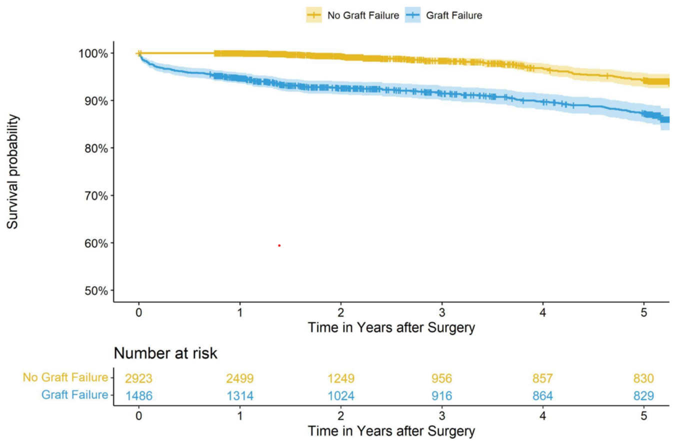

Figure 1: Probability of survival after CABG in patients with no graft failure versus patients with graft failure. Gaudino, Mario, et al. 7 July 2023. AHA Journals, https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.123.064090. Accessed 21 Feb. 2024.

The above graph depicts data collected from the experiment mentioned above. It explores how the mortality risk of patients with graft failure is higher than that of those without.

There are also several risks to angioplasty. The patient could bleed from the blood vessel where the stent was placed or the dye given to the patient during angioplasty may be an allergen. In some rare cases, angioplasty can also lead to a heart attack or stroke.

Therefore, by examining the risks of these procedures, it is clear that we need a surgical method for the removal of plaque that is safer. Scaled-down robots traveling through blood vessels could offer a more accurate and secure way to approach the medication site (Hampson, 2023).

This paper will review newly proposed treatments for atherosclerosis which involve the use of microbots that will enter the arteries. These can be categorized into two main groups - magnetically manipulated and heating strategy. As the names suggest, the former involves penetration into the arterial plaque by a robot that works as a magnetic drilling actuator, and the latter involves penetrating heating for atherosclerosis. This paper will review and examine the following robots, with the following reference names for simplicity:

- Lee et al invented magnetic training actuators (MDAs) and outlined their locomotion and drilling conduct in vascular network-mimicking fluid channels. These robots were tested in a 3D phantom of the coronary artery. The magnet in the magnetic drilling actuator was rotated through a rotating magnetic field. Name: MDAs

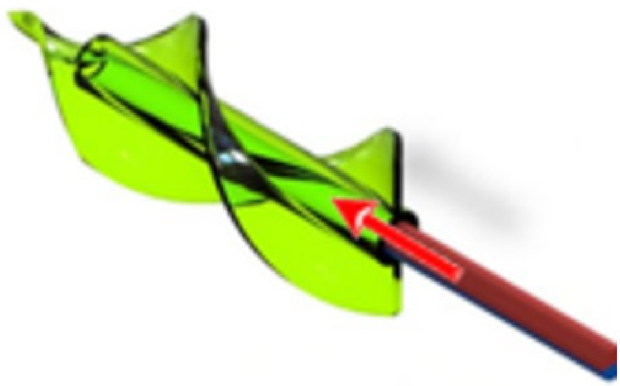

Figure 2: MDAs Lee, Sunkey. MDAs. 27 Feb. 2018. Nature, https://www.nature.com/articles/s41598-018-22110-5. Accessed 11 Feb. 2024.

- Hatem et al constructed a helical robot for penetrating atherosclerotic plaque. This magnetic helical robot was externally actuated. This was tested in artificial plaque phantoms with increasing combined concentrations of gelatin, calcium, carbonate, or hydroxyapatite.Name: Helical robot

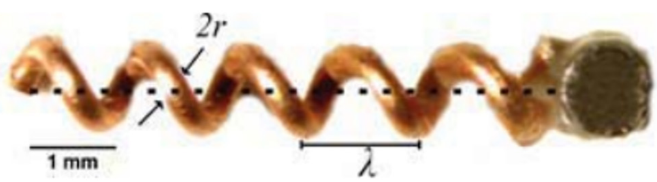

Figure 3: Helical Robot Hatem, Hussein. Helical Robot. July 2020. ResearchGate, https://www.researchgate.net/publication/348166439_Penetration_into_atherosclerotic_plaque_phantoms_using_helical_robots. Accessed 11 Feb. 2024.

- Sa et all developed a separable and recombinable magnetic robot (SRMR) in which an untethered magnetic robot (UMR) can be delivered to a region of a blood vessel with a blockage, performing effective tunneling, and be retrieved with a delivery catheter outside the body. Name: SRMR

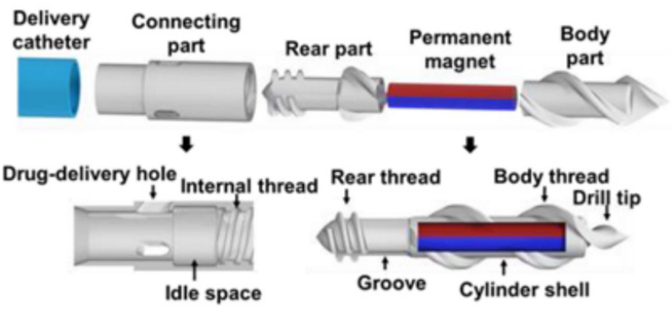

Figure 4: SRMR
Sa, Junchi. SRMR. 9 Feb. 2023. IEEE XPLORE, https://ieeexplore.ieee.org/document/10041766. Accessed 11 Feb. 2024.

- Wang et al constructed a tissue-mimicking phantom in which a polyimide catheter was placed. Electrodes were attached to the outer surface of the catheter to deliver radiofrequency energy to the phantom. They developed radiofrequency balloon angioplasty. Name: Conformational Penetrating Heat Strategy (CPHS)

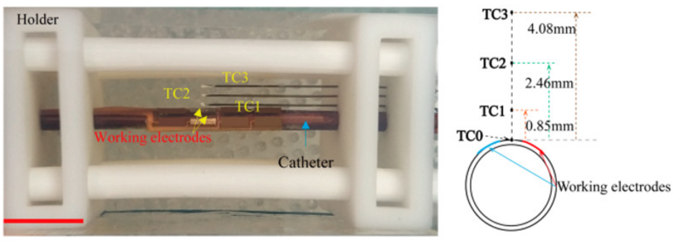

Figure 5: CPHS Wang, Hongying. CPHS. 16 Jan. 2023. National Library of Medicine, https://pubmed.ncbi.nlm.nih.gov/36829656/. Accessed 11 Feb. 2024.

METHODOLOGY

In the methodology, the structure of the robots (which includes the materials and the sensors incorporated), their actuation, and their methods of performing their function will be discussed.

Magnetic Drilling Actuator for Navigation in a Three-dimensional Phantom Vascular Network (Lee et al., 2018)

Key Features of Existing Intravascular Microrobots:

They have an extremely small size (ranging from micrometers to millimeters). As a result, the procedure involving their use is somewhat non-invasive. The microrobots are manipulated wirelessly using an external magnetic field and have a high degree of freedom (DOF) as compared to the guide wire and catheter used in angioplasty which has few DOFs and requires manual navigation by a surgeon. These microrobots were able to demonstrate usefulness in two-dimensional spaces in a horizontal plane.

Key features of the microrobots fabricated by Lee et al (in addition to existing features):

Magnetic drilling actuators (MDAs) with different numbers of spirals facilitate their drilling action in a fluidic environment. This item is manufactured using a 3D printing technique that incorporates a diametrically magnetized neodymium (Nd) alloy magnet. The MDA is fabricated by 3D stereolithography (Proto Labs Inc., USA, n.d.). The MDA has a length of 9mm and a diameter of 3mm. It is spiral-shaped. The MDA has a cylindrical inner space, which hosts a parcelyne-coated Nd magnet with the following dimensions: 0.55mm in length and diameter. This magnet is magnetized in the direction of the diameter. The MDAs were constructed using double, triple, and quadruple spirals.

Key features:

They are manipulated by a rotating magnetic field (RMF). They are characterized by their use and performance in horizontal and vertical planes. The MDA is navigated to a blockage in the vascular network by an external magnetic field after being introduced into the body in a minimally invasive manner. The MDA provides an open pathway for the recirculation of blood by drilling through the thrombus. The MDAs have 5 DOFs (three translational and two rotational) and are controlled using an EMA system, in which the linear superposition of individual fields from eight hemispherically configured electromagnetic coils carrying different currents generates a magnetic field. The magnet in the magnetic drilling actuator was rotated through a rotating magnetic field. Midst of orbit, the MDA could glide forward by a corkscrewing motion. Therefore, the translation velocity can be controlled by adjusting the magnetic intensity and RMF frequency. The swimming or gliding motion of the MDA can be manipulated by changing the pivot of the RMF.

Results:

The MDA with the double spirals moved the fastest, covering a distance of approximately 50mm in 0.3 seconds. The translational velocity of the MDA in both the vertical and horizontal planes was observed to rise as the RMF frequency increased and the number of spirals decreased. The translational velocity was typically lower in the vertical than the horizontal plane. Additionally, the MDA with four spirals showed movement in the horizontal plane but not the vertical plane. These results suggest a greater gravitational force on the MDA in the vertical plane than in the horizontal plane. In order to measure the MDA's navigation in a complex phantom network, where it needs to select a desired path at the junction of multiple channels, the MDA was actuated in a 2D fluidic channel with 45 and 60-degree branches. The MDA adeptly and accurately maneuvered through the branches at 45 and 60 degrees.

Drilling performance of MDAs:

2D and 3D drilling of the magnetic drilling actuators was tested in a vertical tube (4.5mm in diameter) and a 3D phantom of the coronary artery. Each of these was partially occluded by an artificial thrombosis, comprising 1.5% gelatin and 98.5% porcine blood.

Results:

During drilling, the ruptured clot dislodges and MDA enters the blood vessel in approximately 10 seconds. Therefore, the MDA can accurately target thrombi in complex 3D phantom vascular networks under wireless magnetic control.

Biocompatibility of MDAs:

The biocompatibility assessment of the MDA material involved testing it with human colorectal cancer (HCT116) cells. This choice was prompted by the fact that MicroFine, the material resembling acrylonitrile butadiene styrene (ABS) and used in 3D printing the MDA structure, needs more prior investigations regarding its compatibility with biological samples. The study entailed the cultivation of HCT116 cells alongside the MDA material, both in the presence and absence of a parylene coating, within a 96-well plate for a duration of one day. Subsequently, cell viability was determined through fluorescence imaging and compared against the control group, which comprised HCT116 cells without the presence of the MDA material.

Results:

The viability of the cells exceeded 95% across all experimental conditions, showing no significant difference when compared to the control group.

Penetration into atherosclerotic plaque phantoms using helical robots (Hatem et al., 2020)

The helical robot, its propulsion, and the fabrication of the plaque phantom:

A permanent magnet-based robotic system with two synchronized rotating dipole fields actuates the helical robot. The helical robot is propelled inside the catheter segment containing the plaque phantom by the two external rotating magnets. Each magnet is a neodymium magnet (NdFeB). The helical robot inside the catheter comprises a magnetic head, a NdFeB magnet which is 1mm in diameter, and a helical body. The tail consists of a copper wire coiled into a helical spring and attached rigidly to the head. Dimensions of the helix: (Length: 6mm, Turns: 5, Filament radius: 0.3mm). The phantoms of plaque are prepared consisting of gelatin and calcium salt (either calcium carbonate or hydroxyapatite). The gelatin serves to imitate collagen in atherosclerotic plaque. The calcium salt serves to imitate the calcium content in the plaque. Their percentages were varied.

Penetration into plaque phantoms:

The robot in the catheter starts moving towards the target phantom when the two external permanent magnets are rotated. The actuation frequency of the helical robot is 8 Hz and the length of the plaque phantom is approximately 4cm for all trials.

Results:

Rheology results: Changing the gelatin concentration has a significant effect on the mechanical properties of the plaque rather than a change in calcium concentration.

The elastic modulus of the fabricated phantoms of plaque has a comparable modulus to aortic plaques tested under compression in conducted studies (Lee et al.) The results for the calculated speed for the robots showed a high standard deviation in the gelatin-HA samples. Therefore, a high number of trials were conducted. Not all the trials had successful penetration into the phantoms. Some samples were more resistant to the robot traveling the entire length of the phantom, resulting in incomplete penetration. As per the results, the robot achieves its highest speed with a moderately stiff sample. This indicates that the robot is best suited for a low to moderately calcified sample. The speed of the robot decreases as the gelatin percentage increases (for the sample with calcium carbonate). The penetration speed of the robot in gelatin-HA samples was significantly lower. As the gelatin concentrations in the samples increase, the robot speed decreases due to a higher strength and higher stiffness material.

Separable and Recombinable Magnetic Robot for Robotic Endovascular Intervention (Sa et al., 2023)

Structure and Fabrication of the Separable and Recombinable Magnetic Robot (SRMR):

The SRMR consists of a delivery catheter and an untethered magnetic robot (UMR). The delivery catheter utilizes a screw mechanism and a rotating external magnetic field (EMF) to separate and recombine with the UMR. The UMR is composed of three parts: a body part, a permanent magnet, and a rear part. The body part is designed with a double-threaded structure to maximize the thrust force generated by the rotating EMF. The permanent magnet is used to generate the magnetic torque of the UMR. The UMR rotates freely within an idle space of the connecting part to prevent distortion of the catheter or fracture of the connecting part. An axial groove in the rear part of the UMR minimizes the possibility of disconnection of the UMR from the delivery catheter due to the fluid impact. The body and rear parts of the UMR and the connecting part of the delivery catheter comprise photocurable dental resin satisfying biocompatibility; they were manufactured via 3D printing in digital light processing (DLP). The permanent magnet inserted into the UMR was an N55 neodymium magnet with a diameter and length of 1 mm and 5 mm, respectively. It was radially magnetized, coated with a Parylene C on the outside, and completely wrapped with a dental resin for biocompatibility.

Manipulation Method of the Magnetic Navigation System:

The robotically adjustable magnetic navigation system for endovascular intervention (I-RAMAN system), which comprises a magnetic navigation system (MNS) and feeding robot was used (Intermag, n.d.). The desired magnetic field can be generated in the region of interest (ROI) by controlling the current applied to eight electromagnets of the MNS.

Steering, Separating, and Tunneling Motion of the SRMR:

The above functions can be achieved using the magnetic torque generated by the interaction of the permanent magnet and the EMF generated by the MNS. During the steering motion, the UMR is not separated from the delivery catheter. After the UMR reaches the vicinity of a lesion using the delivery catheter, it can be separated from the delivery catheter to reach the target lesion closely and perform vascular tunneling. Finally, the separated UMR can tunnel an occlusive blood vessel at a high rotating speed. After tunneling, the blood clot particles can be aspirated through the internal hole of the delivery catheter to prevent

embolism.

Recombining Motion of the SRMR:

After the UMR completes the tunneling function in the occlusive lesion, it should be retrieved from the patient's body. In this case, a rotating EMF is generated opposite the separation motion. When recombining the UMR with the connecting part of the delivery catheter, the central rotation axis of the UMR must be maximally centered with the central axis of the connecting part to safely recombine the SRMR, which is significantly more complex than separation.

Results:

The steering motion of the SRMR and the separating, tunneling, and recombining motions of the UMR were verified in a mimetic vascular model with a pseudo blood clot of 0.5 wt% agar. The vascular model comprised 6-mm diameter glass tubes with two 60° branches and a 4-mm diameter straight tube with a blood clot, which covers the diameter of human arteries commonly subject to occlusive thrombosis. When the SRMR reached the branch of the vascular model after entering the glass tube, steering was performed by sequentially applying a magnetic field with an angle of 30° to the x-axis. After applying a magnetic field with an angle of 135° and successful entry into the desired direction, a magnetic field with an angle of 150° to the x-axis was applied to the second branch to enter the straight tube. After a magnetic field with an angle of 90° was applied and the SRMR reached the occlusive lesion, the UMR was separated by rotating the EMF counterclockwise at 10 Hz to rotate it in the forward direction. Subsequently, the frequency was increased to 20 Hz to perform tunneling motion, and the fragments of pseudo blood clots generated after tunneling were sucked through the hole of the delivery catheter.

A New Conformal Penetrating Heating Strategy for Atherosclerotic Plaque (Wang et al., 2023)

Current methods to reach penetrating heating for atherosclerosis for two together marks, that are the specified protection depth to preserve the endothelial coating and the ablation depth to accomplish the eradication of plaque, cannot be used as the depth of the plaque and the diameter of the endothelial layer change. This experiment was administered to question the effects of the control parameters, the target temperature (Ttarget), the cooling water temperature (Tf), and the cooling water velocity (Vf). In order to conduct a more quantitative analysis and assessment of the ablation depth and the preservation depth of the control specifications, a three-dimensional model was developed. In addition, a conformal penetrating heating approach was suggested based on the mathematical results.

This experiment uses the information of the structure of a plaque to construct its model. A standard plaque is characterized by the presence of a necrotic core, proliferating smooth muscle cells (SMCs), and an overlying intima. The necrotic core along with the proliferating SMCs represents the undesirable tissue that requires ablation, whereas the intima, which consists of a delicate endothelial layer, should be preserved. The target temperature for proliferated SMCs is over 50 degrees Celsius, while the temperature in the whole layer of the intima should be under 50 degrees Celsius. This indicates that varying requirements for protection depth and distinct thermal gradients are necessary within the intima.

Structure and fabrication of the model (including the robot and the phantom):

In this paper, they used a tissue-mimicking phantom and arterial tissue-mimicking deionized water. The model consists of a polyimide catheter with an inner diameter of 2.5mm and an outer diameter of 2.94mm. This is meant to simulate an angioplasty balloon. The experiment involved placing the model into the tissue-mimicking phantom, which was placed in a 37°C thermostat water bath. For each period, a singular pair of electrodes was used to give the 460 kHz radiofrequency energy to the phantom. However, there were 3 × 4 electrodes (breadth and spacing: 1 mm, length: 4 mm) joined to the exposed surface of the catheter. The host computer regulated the homemade radiofrequency source, which was calibrated accompanying an oscilloscope, and the alterable-speed pump by means of a data procurement tool.

Three calibrated temperature sensors (TC1, TC2, and TC3) were placed in a tissue-mimicking phantom parallel to the catheter to monitor phantom temperature in depth. TC1, TC2, and TC3 may denote the sites of plaque, adventitia, and adjacent tissue.

A thermocouple (TC0) was placed on the inner surface of the tissue phantom to measure temperature at the control point (Ttarget). The sensors were insulated with thin polyimide tubes and covered with thermally conductive silicone grease to reduce electromagnetic interference and minimize interference in temperature measurement. (research how these materials provide biocompatibility)

Experimental heating conditions:

A series of three experimental groups were established to investigate the effects of the three parameters under consideration (Ttarget, Tf, Vf).

In the first group, Ttarget was maintained at 35°C, 38°C, 40°C, 43°C, 45°C, and 48°C, with Tf fixed at 15°C and Vf at 2.85 m/s.

The second group involved varying Tf from 10°C to 30°C in increments of 5°C, while Ttarget was held constant at 38°C and Vf remained at 2.85 m/s.

In the third group, Vf was modified from 1.51 m/s to 4.57 m/s in 0.76 m/s increments, with Ttarget set at 38°C and Tf at 20°C.

The experiment included two stages: a 45-second expansion of the balloon using cooling water and 2 minutes of convection cooling combined with RF heating. Temperatures (TC2, and TC3) with Keysight DAQ970A. Temperature T0 served as the control point. Each experiment was repeated three times.

Results:

The study found that temperature changes at three monitoring points in tissue, including plaque, adventitia, and surrounding tissue, were linearly influenced by control parameters. The

main factors affecting ablation results were Ttarget and Tf, which affected ablation depth and protection depth. The study found that RF volumetric heating power and convection cooling power were affected by Ttarget and Tf, allowing bidirectional control of confined penetrating heating. The existing RF electrodes and cooling agent configuration demonstrated the capability to achieve an ablation depth between 0.47 mm and 1.43 mm, while the protection depth varied from 0 mm to 0.26 mm, adequately addressing the needs of most arterial plaques. When utilized independently, these two parameters exert opposing influences on the regulation of ablation and protection depths. However, by employing both parameters concurrently, a comprehensive ablation range that meets the majority of clinical plaque treatment demands can be realized. The viable combinations of these conditions have been identified.

DISCUSSION

In this component of the paper, there will be a detailed comparison of the robots, their suitable and unsuitable features, and what changes can be made to advance at a greater pace toward a future with robots treating atherosclerosis.

The questions that the discussion answers or the features of the robots that it analyses which can determine their practicality and safety are entry and removal, storage of plaque, maneuverability, biocompatibility, intervention, duration, and frequency.

Entry and Removal

Beginning with the MDA, it has been constructed in such a way that it can be inserted and removed with ease from the bloodstream. It works on the principle of an external magnetic field, ensuring a smooth entry and exit. The MDA can be extracted easily after the procedure by the use of a catheter. The entry and exit are facilitated by wireless control and retractive abilities. As for the Helical Robot, the author states that the robot can be inserted and removed without causing significant damage to the surrounding blood vessels. Moving on to the SRMR, its entry is characterized by an external magnetic field. The SRMR can separate the untethered magnetic robot (UMR) from the delivery catheter using a counterclockwise rotating EMF, allowing the UMR to tunnel through the occlusive lesion.

To exit, the UMR recombines with the delivery catheter. Next is the CPHS. A balloon catheter system is discussed that can deliver penetrating volumetric heating to the atherosclerotic plaque while providing surface cooling to protect the endothelial layer. As for the removal of the balloon catheter system, the paper does not specify any such strategy.

Plaque removal

The MDA, upon penetrating the plaque, allows it to flow through a newly created passage rather than storing it. It is mentioned in the paper that the MDA penetrated the artificial thrombosis model, allowing the porcine blood to flow through the thrombosis and mix with the surrounding DI water. The helical robot, despite its success in penetration of atheroma, has not been mentioned to store or pass the plaque out immediately. The paper does not explicitly state what happens to the removed plaque material. The paper that discusses the SRMR fails to capture the fate of the arterial plaque after the SRMR tunnels through the occlusive lesion. The paper regarding the CPHS does not explicitly mention what happens to the removed plaque.

Maneuverability

The MDA has been designed with exceptional maneuverability. The MDA can be exactly manipulated in each horizontal and vertical plane using an external magnetic field, permitting it to choose and move via favored paths at junctions of multiple channels. The MDA was able to accurately navigate a synthetic 3-D vascular network phantom and selectively circulate through unique branches to attain the thrombosis blockage. in comparison to standard guidewire-based processes that have restricted degrees of freedom, the wireless magnetic control of the MDA affords five degrees of freedom (3 translational, 2 rotational) for improved maneuverability. The MDA's spiral design and corkscrewing motion generated by the rotating magnetic area contribute to its locomotion and potential to navigate through the vascular network. The helical robot has a small, flexible, and soft structure that enables efficient navigation through complex vascular networks, in addition to its ability to conform to the shape of blood vessels and make tight turns. The use of an EMF for the SRMR permits efficient change of directions to reach the target lesion. Upon separation, the UMR can attain high frequencies, facilitating smooth and swift movement. As the CPHS is a heating strategy rather than a robot, it does not particularly require maneuverability. However, the relatively small diameter suggests the catheter may have reasonable maneuverability to navigate through the vasculature and reach the target atherosclerotic lesions. The catheter also has a microelectrode array embedded on its surface, which indicates it has a degree of conformability to adapt to the vessel geometry.

Biocompatibility

The MDA was fabricated using an acrylonitrile butadiene styrene (ABS)-like material called MicroFine. To test the biocompatibility, human colorectal cancer (HCT116) cells were cultured with the MDA material, both with and without a parylene coating. The results showed that cell viability was over 95% in all experimental conditions, and did not differ significantly compared to the control group without the MDA material. This indicates the MDA material did not exert a cytotoxic effect on the cells. The extensive biocompatibility is furthered by The use of parylene, a biocompatible material, to coat the neodymium (Nd) magnet core of the MDA. As for the helical robot, the paper emphasizes that the robot is designed to be highly biocompatible, with materials and structures that are safe for use within the human body. The paper also notes that the robot is designed to minimize any potential inflammatory or thrombogenic responses from the body, further enhancing its biocompatibility. In an experiment on a female miniature swine, the SRMR was able to be safely introduced and operated within the animal's vascular system without any reported adverse effects. The SRMR was able to perform its functions without causing harm to the animal. However, the paper doesn't give any details on the materials used for the robot or delivery

catheter, which is important for assessing the biocompatibility of the system.

For the CPHS, the paper mentions that the catheter is made of polyimide material [3]. Polyimide is a widely used biomaterial known for its biocompatibility, flexibility, and chemical resistance, making it suitable for medical device applications. The use of metallic electrodes, such as copper, raises some potential biocompatibility concerns, as metals can interact with biological tissues and potentially cause inflammatory responses or toxicity.

Intervention/Invasiveness

The MDA is designed to be a minimally invasive intervention, as it can be wirelessly controlled and manipulated using an external magnetic field. This minimally invasive approach contrasts with more invasive procedures like coronary angiography, where the guidewire and catheter move along the vessel wall instead of the center. The paper acknowledges that more research is needed to evaluate the damage caused by the MDA and compare it to existing techniques. The paper associated with the helical robot presents a minimally invasive procedure, which can be an alternative to current treatment methods, limited by rigid endovascular devices and the risks of open surgical procedures. For the SRMR, the paper highlights the SRMR's advanced intervention features that could contribute to improved treatment of atherosclerosis. However, it does not mention the dangers of intervention. For the CPHS, the paper indicates that the proposed treatment approach involves a minimally invasive, catheter-based intervention.

Duration and Frequency

In the 2D vertical tube test, the MDA was able to penetrate the artificial thrombosis model in around 4 seconds by applying a rotating magnetic field at 15 mT. When testing the MDA in the 3D phantom vascular network, the MDA was able to penetrate the thrombosis model in the 3D phantom in approximately 10 seconds. This demonstrates effective drilling in a short duration. The paper regarding the helical robots does not explicitly mention the duration of a single intervention, but the flexibility and maneuverability of the soft robot imply that the procedure could be performed in a relatively short time compared to more invasive surgical approaches. For the SRMR, The UMR can be successfully separated from the delivery catheter within 20 seconds when the magnetic flux density of the EMF is between 5-10 mT and the rotation frequency is greater than 7 Hz. This presents a relatively long duration within the bloodstream, with no mention of frequency. The duration and frequency of the CPHS has not been mentioned in the paper.

	Entry and removal	Plaque removal	Maneuverability	Biocompatibility	Invasiveness	Duration and frequency
MDA	Approved	Approved	Approved	Approved	Approved	Approved
Helical Robot	Approved	Not approved	Approved	Approved	Approved	Not approved
SRMR	Approved	Not approved	Approved	Partially approved - lack of information	Not approved	Partially approved - lack of information
CPHS	Entry approved, not removal	Not approved	Not approved	Partially approved - lack of information about the use of metals	Approved	Not approved

Table 1: A discussion of important factors across the different robots

From the above table, it is evident that the MDA checks all necessary criteria, making it the most appropriate model for the penetration of arterial plaque.

Future Outlook

Finances: The high cost of developing and deploying soft robots for atherosclerosis treatment is a major barrier to widespread adoption. However, as the technology matures and manufacturing processes improve, costs are expected to decrease significantly (Meng et.al, 2024).

Plaque removal: A key challenge is safely removing the plaque after the soft robot penetrates the arterial blockage. Ideally, the plaque would be liquefied or broken into small enough pieces to be flushed out by the bloodstream without causing further clots or damage (Meng et.al, 2024).

Vision systems: Equipping soft robots with miniaturized cameras, sensors, and imaging capabilities will be transformative for atherosclerosis treatment (Roche et.al, 2017). Wireless data transmission from the robot to an external console will be needed to enable this functionality (Rosalia et.al, 2023).

Autonomy: Aiming at performing these procedures by less skilled surgeons in an effort to make them cheaper is the main goal. Technological development in robotics and artificial intelligence for autonomous navigation and control also makes it easier for soft robots to enter arteries and eliminate cholesterol without human interaction. Another advantage would be if the numerous phases that are a part of the procedure are combined into a single robotic equipment. More guidance and simpler interfaces in the system training will be crucial to expand the usage of these systems among medical workers.

Procedure Duration and Recovery

Minimizing the duration of the atherosclerosis treatment procedure and the patient's recovery time will improve outcomes and reduce costs.

CONCLUSION

Atherosclerosis is a widespread disease, which continues to kill several individuals. In such a world, if there were a new and

innovative engineering solution, it should be a microrobot that could enter the arteries and extract the atherosclerotic plaque in a non-invasive or minimally invasive manner. Robots are being developed to combat atherosclerosis. However, none have been actualized, and it remains a problem in many communities. These robots could be distributed to rural areas. Since the procedure involving their use is minimally invasive, medical professionals with little experience could carry it out safely, allowing millions of people to be cured every year. Therefore, this review paper allows an active pursuit of this engineering solution by analyzing and proposing models that are in the study. From the results, the MDA approved all areas of importance for a soft robot to combat atherosclerosis. Therefore, this study advocates for further research into its practicality, with the future outlook of launching it. To further progress in this field, developing cheaper materials and autonomous robots would allow rural areas to benefit from this creation, which does not always have the luxury of experienced doctors to control and guide the robots. In conclusion, this area of study is highly essential for the treatment of a disease that has no definite solution as of now, but a newfound treatment could save the lives of millions.

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